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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/893,443	06/29/2001	Michael Gmachl	0652.2310001/EKS/SEZ	6378

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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT PAPER NUMBER

1642

DATE MAILED: 03/28/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/893,443

Applicant(s)

GMACHL ET AL.

Examiner

Christopher H Yaen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 June 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 3-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Nasmyth *et al.* (WO 98/21326). The claims of the instant application are drawn to a method of identifying inhibitors of the ubiquitination reaction mediated by APC, wherein the method includes: APC11 (claim 1); APC11, E1, E2, ATP, and ubiquitin (claim 3); and APC11, E1, E2, ATP, ubiquitin, and a substrate protein. Nasmyth *et al.* also disclose of a method to identify substances that interfere with APC, wherein their method includes all of the components of the instant invention. Therefore, the methods disclosed in the instant application are anticipated.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nasmyth K *et al.* (WO 98/21326), in view of Kirschner *et al.* (WO 96/33286), and further

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in view of Hatfield PM *et al.* (J. Biol Chem 1990 Sep 15;265(26):15813-7) and Gonen H *et al.* (J. Biol Chem 1999 May 21;274(21):14823-30).

Claims 1-27 are drawn to a method for identifying a compound that inhibits the ubiquitination reaction mediated by a subunit of APC, namely APC11, wherein the method involves incubating APC11 (E3), an E1 enzyme, an E2 enzyme, ubiquitin, ATP and in some cases (claims 4, 7, 10, 13, 16, 19, 22, 25-27) a substrate, in the presence or absence of a compound that inhibits the said reaction, followed by measuring the compounds ability to perform said reaction.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Nasmyth K *et al.* disclose of a compound screening method involving the incubation of APC11 as the E3 enzyme, E1 enzyme, and E2 enzyme, ATP and a substrate (cyclin B), followed by the measuring of the ubiquitination process. Nasmyth *et al.*, however, do not specifically disclose of the E1 and E2 enzymes, and or the assessment of the reaction either in the presence or absence of an ubiquitination reaction.

Kirschner *et al.*, do disclose a process for identifying agents that are capable of inhibiting ubiquitination events involving a subunit of APC (E3), an E1 enzyme, E2

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enzyme, ubiquitin, ATP, and a substrate, in the presence or absence of said agent, wherein the presence or absence of the said agent to ubiquitinate is measured.

Kirschner *et al.* also disclose of ubiquitinating a substrate.

Hatfield *et al.* do disclose of an E1 enzyme, UBA1, and describe its isolation and use as an activating enzyme in the ubiquitination process.

Gonen H *et al.* do disclose of an E2 enzyme, UBCH5b, and describes its function as a conjugating enzyme, in the ubiquitination process.

Therefore it would have been obvious to one of ordinary skill at the time the invention was made to conceive of a method to screen for compounds that inhibit APC ubiquitination involving the use of a subunit of APC, APC11, as the E3 enzyme, in the presence of E1 and E2 enzymes, ATP, and in some cases the presence of a substrate (claims 4, 7, 10, 13, 16, 19, 22, 25-27). One of ordinary skill in the art would know to combine these references to arrive at the claimed invention, because it was known in the art at the time the invention was made that a screening method involving components similar to those disclosed in the instant invention, were used to screen for inhibitors of APC, specifically APC11 (Nasmyth K *et al.*). One of ordinary skill in the art would also know to assess the ubiquitination reaction by measuring the process either in the presence or absence of an agent/compound (Kirschner *et al.*). In addition, the E1 and E2 enzymes used by both Nasmyth *et al.* and Kirschner *et al.* could have been substituted with any E1 or E2 enzyme, because it was well known in the art, that these enzymes were being used as parts of the *in vitro* ubiquitination process (Hatfield *et al.* and Gonen *et al.*). Furthermore, the instant application, states "one of ordinary skill in

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the art...by modifying or changing the invention with a wide and equivalent range of conditions, formulations, and other parameters...", therefore, one of ordinary skill at the time the invention was made would know to substitute the components as the art was updated with new discoveries. One of ordinary skill in the art would expect a reasonable amount of success in doing so because, others have shown it is possible to measure and find inhibitors of ubiquitination mediated by APC.

Conclusion

5. No claims are allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

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Christopher Yaen

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March 21, 2002



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